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EXAMINER	
DIAMOND, ALAN D	
ART UNIT	**PAPER NUMBER**
1753	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/052,931	NOUADJE ET AL.	
	Examiner	Art Unit	
	Alan Diamond	1753	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-5,7-25,27-30 and 33* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-25,27-30 and 33* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *18 January 2002* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Comments

1. The objection to the abstract has been overcome by applicant's amendment thereof.

2. The objections to claims 1 and 12 for informalities has been overcome by Applicant's amendment thereof.

3. The rejection of claims 9, 15, and 26 under 35 USC 112, second paragraph, has been overcome by Applicant's amendment of these claims.

4. The 35 USC 102(b) rejection over JP 2-12059 (JP '059) has been overcome by Applicant's amendment of claims 24 and 25 so as to require that the buffer system has a pH between 9 and 11. JP '059 uses a pH of 4 to 5.

5. Upon reconsideration, the 35 USC 103(a) art rejection based on Lauer et al in view of Alter et al are expressly withdrawn by the Examiner. As noted below, Alter et al, alone, has been used to anticipate the solution in instant claims 24, 25, 27, 29, and 33. Alter et al differs from the methods in claims 1, 20 and 21 since Alter et al teaches a sample storage buffer or a diluent buffer for the protein sample prior to capillary zone electrophoresis. The capillary that Alter et al's protein constituent is passed into does not contain a buffer system containing the instant additive, but rather contains a typical running buffer such as a borate buffer (see col. 9, lines 55-56; and col. 10, lines 50-51). In other words, Alter et al does not pass the least one protein constituent into a capillary containing the instant buffer system, but rather adds to the capillary a protein constituent that is in a buffer system (storage or diluent) containing the instant additive

(see also col. 10, lines 21-26). Said additive is not in the capillary before the protein sample is added. Indeed, even between runs, Alter et al cleans the capillary (see col. 9, lines 57-59).

6. The rejections under 35 USC 102(b) and 103(a) over Hjerten et al are withdrawn by the Examiner so as to reduce the number of issues in the instant application.

Specification

7. The disclosure is objected to because of the following informalities: On page 6, at line 9, the term "en" should be deleted. Appropriate correction is required.

Claim Objections

8. Claims 1, 8, 9, 19, and 24 are objected to because of the following informalities: In claim 1, at line 4, there should be a comma after the word "albumin". In claim 8, at line 1, the word "that" should be deleted. In claim 9, at line 5, the term "di-or" should be changed to "di- or". In claim 19, at line 3, the term "caesium" should be changed to "cesium". In claim 24, at line 4, the term "Li-" should be changed to "di-". Appropriate correction is required.

9. Claim 3 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim, or amend the claim to place the claim in proper dependent form, or rewrite the claim in independent form. Claim 3 does not further limit parent claim 1 because the proteins listed in claim 1 are biological materials. Thus, the sample in claim 1 is a biological sample. Thus, by specifying that the sample is a biological sample, claim 3 is setting forth what is already inherent in claim 1.

Claim Rejections - 35 USC § 112

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claim 25, 29, 30, and 33 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 25 is now indefinite because it sets forth a list of compounds at lines 3-9 from which the additive is selected, and yet, at lines 9-14, sets forth that the additive is one "comprising a hydrophobic portion composed of at least one linear or non linear alkyl chain containing 4 to 22 carbon atoms, and/or at least a combination or 1 to 10 cyclic aromatic groups or cyclic non-aromatic groups, and an anionic pole comprising at least one group selected from sulphonates, carboxylates, sulphates, phosphates and carbonates". Thus, claim 25 sets forth a range within a range for the additive, and the meets and bounds for the claim cannot be determined. The same applies to dependent claims 29, 30, and 33. It is suggested that applicant delete "comprising a hydrophobic portion composed of at least one linear or non linear alkyl chain containing 4 to 22 carbon atoms, and/or at least a combination or 1 to 10 cyclic aromatic groups or cyclic non-aromatic groups, and an anionic pole comprising at least one group selected from sulphonates, carboxylates, sulphates, phosphates and carbonates" from lines 9-14 of claim 25.

Claim Rejections - 35 USC § 102

12. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

13. Claims 1-3, 7-10, 12, 13, 16-21, 23-25, 27, 29, and 33 are rejected under 35 U.S.C. 102(b) as anticipated by Lauer et al, "Capillary Zone Electrophoresis of Proteins in Untreated Fused Silica Tubing," Anal. Chem., Vol. 58, pages 166-170, (1986).

With respect to independent claims 1, 20, 21, 24, and 25, Lauer et al teaches a buffer system in water for capillary zone electrophoresis of a protein mixture, wherein the buffer system comprises, at pH 9.22, 20 mM CHES buffer, i.e., (cyclohexylamino)ethanesufonic acid buffer, which reads on both the instant buffer and the instant additive (i.e., reads on the instant C_6 to C_{22} alkyl-monosulfonate additive) (see the experimental section at page 167; and Figure 2 at page 168). The proteins separated in Figure 2 at page 168 include conalbumin and ovalbumin, which are "albumin" as in instant claims 1, 20, and 21. It is the Examiner's position that said CHES buffer has a hydrophobic interaction with the conalbumin and ovalbumin (i.e., with albumin) and provides the conalbumin and ovalbumin with at least one negative charge thereby modifying the electrophorectic mobility. CHES has an anionic pole (from the sulfonic acid group) with a pH of more than 9 and a hydrophobic portion, from the (cyclohexylamino)ethane group. Indeed, CHES is mentioned on page 6, line 19, of the instant specification as an example of the instant additive. With respect to claim 24, the water that the CHES buffer is in reads on the instant support.

With respect to claim 2, the protein constituents in Lauer et al's mixture are separated and detected (see Figure 2 at page 168).

With respect to claim 3, the proteins in Lauer et al's mixture are biological materials, and thus, the mixture constitutes a biological sample.

With respect to claims 7 and 8, and as noted above, CHES has an anionic pole (from the sulfonic acid group) and a hydrophobic portion, from the (cyclohexylamino)ethane group.

With respect to claims 9, 10, 27, and 29, and as also noted above, CHES reads on the instant C_6 to C_{22} alkyl-monosulfonate additive. CHES is a C_8 alkylsulfonate.

With respect to claims 12 and 13, the CHES has a concentration of 20 mM (see Figure 2 at page 168). It is the Examiner's position that the 20 mM CHES does not exceed the critical micellar concentration of the CHES.

With respect to claim 16, the pH is 9.22 (see Figure 2 at page 168).

With respect to claim 17, the capillary tube is fused silica (see the title, abstract, and the experimental section at page 167).

With respect to claims 18 and 19, NaOH or HCl is used for adjusting pH (see the paragraph bridging the left and right column on page 167).

With respect to claims 23 and 33, said CHES is a zwitterionic biological buffer.

Since Lauer et al teaches the limitations of the instant claims, the reference is deemed to be anticipatory.

14. Claims 24, 25, 27, 29, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Keo et al, U.S. Patent 5,599,433.

Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens, wherein the buffer system is a solution that contains, for example, 100 mM CAPS, i.e. 3-cyclohecylamino-1-propanesulfonic acid (which reads on the instant zwitterionic biological buffer and additive), 300 mM sodium borate (which is a buffer), and NaOH for adjusting the pH to 11 (see col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). It should be noted that CAPS is C_9 alkylsulfonate. Alternatively, the pH can be at 10 (see col. 10, line 46). It is noted that the instant specification teaches, at page 6, lines 17-20, that CAPS is an instant additive. The water in Keo et al's buffer system reads on the support in claim 24. Since Keo et al teaches the limitations of the instant claims, the reference is deemed to be anticipatory.

15. Claims 24, 25, 27, 29, and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Alter et al, U.S. Patent 5,753,094.

Alter et al's running buffer for capillary electrophoresis is borate at pH 10.0 (see col. 9, lines 55-56; and col. 10, lines 50-51). The water in this buffer reads on the support in claim 24. To the running buffer is added a sample containing TES, i.e., 2-[tris(hydroxymethyl)methyl]amino-ethanesulfonic acid, which is a zwitterionic biological buffer that is C_6 alkyl sulfonate and reads on the instant additive (see col. 6, lines 1-16; and col. 11, lines 1-38). It is the Examiner's position that in Examples 2 and 3 at col. 11, the running buffer plus injected sample in the column is still at pH 10, buffered by the running borate buffer. It is the Examiner's position that said TES has a hydrophobic interaction with albumin because it is identical in structure to the instantly claimed

additive. Furthermore, TES has an anionic pole from the sulfonate with a pH of more than 9, and a hydrophobic portion from the 2-[tris(hydroxymethyl)methyl]amino-ethane portion. Since Alter et al teaches the limitations of the instant claims, the reference is deemed to be anticipatory.

Claim Rejections - 35 USC § 103

16. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

17. Claims 1-3, 7-10, 12-21, 23-25, 27, 29, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lauer et al, "Capillary Zone Electrophoresis of Proteins in Untreated Fused Silica Tubing," Anal. Chem., Vol. 58, pages 166-170, (1986).

With respect to independent claims 1, 20, 21, 24, and 25, Lauer et al teaches a buffer system in water for capillary zone electrophoresis of a protein mixture, wherein the buffer system comprises, at pH 9.22, 20 mM CHES buffer, i.e., (cyclohexylamino)ethanesufonic acid buffer, which reads on both the instant buffer and the instant additive (i.e., reads on the instant C_6 to C_{22} alkyl-monosulfonate additive) (see the experimental section at page 167; and Figure 2 at page 168). The buffer system further contains KCl (see Figure 2 at page 168). The proteins separated in Figure 2 at page 168 include conalbumin and ovalbumin, which are "albumin" as in instant claims 1, 20, and 21. It is the Examiner's position that said CHES buffer has a hydrophobic interaction with the conalbumin and ovalbumin (i.e., with albumin) and provides the conalbumin and ovalbumin with at least one negative charge thereby

modifying the electrophorectic mobility. CHES has an anionic pole (from the sulfonic acid group) with a pH of more than 9 and a hydrophobic portion, from the (cyclohexylamino)ethane group. Indeed, CHES is mentioned on page 6, line 19, of the instant specification as an example of the instant additive. With respect to claim 24, the water that the CHES buffer is in reads on the instant support. Other proteins that can be separated by Lauer et al's capillary zone electrophoresis are beta-Lactoglobulins A and B, which encompass the instant beta-globulin (see Table I at page 167 of Lauer et al).

With respect to claim 2, the protein constituents in Lauer et al's mixture are separated and detected (see Figure 2 at page 168).

With respect to claim 3, the proteins in Lauer et al's mixture are biological materials, and thus, the mixture constitutes a biological sample.

With respect to claims 7 and 8, and as noted above, CHES has an anionic pole (from the sulfonic acid group) and a hydrophobic portion, from the (cyclohexylamino)ethane group.

With respect to claims 9, 10, 27, and 29, and as also noted above, CHES reads on the instant C_6 to C_{22} alkyl-monosulfonate additive. CHES is a C_8 alkylsulfonate.

With respect to claims 12 and 13, the CHES has a concentration of 20 mM (see Figure 2 at page 168). It is the Examiner's position that the 20 mM CHES does not exceed the critical micellar concentration of the CHES.

With respect to claim 16, the pH is 9.22 (see Figure 2 at page 168).

With respect to claim 17, the capillary tube is fused silica (see the title, abstract, and the experimental section at page 167).

With respect to claims 18 and 19, NaOH or HCl is used for adjusting pH (see the paragraph bridging the left and right column on page 167).

With respect to claims 23 and 33, said CHES is a zwitterionic biological buffer.

Lauer et al teaches the limitations of the instant claims other than the difference which is discussed below.

With respect to claims 14 and 15, Laurer et al does not specifically teach that its CHES buffer concentration can be 1 mM to 4 mM, e.g., about 2.5 mM, instead of the 20 mM that is used in Figure 2 at page 168. However, Lauer et al is not limited to the 20 mM. Any concentration of CHES buffer that would provide buffering is within its purview. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a lower concentration of the CHES buffer, i.e., to have used a CHES buffer concentration of, for example 4 mM or 2.5 mM, to perform Lauer et al's capillary zone electrophoresis because Lauer et al is not limited to the 20 mM, and any concentration of CHES buffer that would provide buffering, such as 4 mM or 2.5 mM is within its purview.

18. Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lauer et al as applied to claims 1-3, 7-10, 12-21, 23-25, 27, 29, and 33 above, and further in view of Karger et al (U.S. Patent 4,778,909).

Laurer et al is relied upon for the reasons recited above. In its study to show that that it is possible to perform capillary zone electrophoresis of proteins, Lauer et al chose

proteins to cover a wide range of isoelectric points and molecular weights (see abstract; the Reagents section at page 167; and Table I). Lauer et al teaches the limitations of instant claim 5, the difference being that none of the proteins tested in Table I at page 167 is a blood protein. Karger et al is relied upon for showing that human transferrin (i.e., human β_1-globulin), which is a blood protein, has a pI 5.0 and a molecular weight of 77,000 (see Table VIII at col. 19). Karger et al also shows that bovine serum albumin (BSA), which also is a blood protein, has a pI of 4.4 to 4.8 and a molecular weight of 68,000 (see Table VIII at col. 19). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used human transferrin or BSA as a protein for Lauer et al's capillary zone electrophoresis because these proteins have pI values (as shown by Karger et al) within the range of pI values set forth in Table I of Laurer et al. While it is true that said human transferrin and BSA have higher molecular weights than those in Lauer et al's Table I, it should be noted that Lauer et al is not limited to the protein molecular weights in said Table I.

19. Claim 22 is rejected under 35 U.S.C. 103(a) as being unpatentable over Lauer et al as applied to claims 1-3, 7-10, 12-21, 23-25, 27, 29, and 33 above, and further in view of Ohmura et al, U.S. Patent 5,521,287.

Lauer et al, as relied upon for the reasons recited above, teaches the limitations of claim 22, the difference being that Lauer et al et al does not specifically teach the use of sodium sulfate in place of said KCl. Ohmura et al teaches that salts for adjusting ionic strength include KCl and sodium sulfate (see the paragraph bridging cols. 7 and 8). It would have been obvious to one of ordinary skill in the art at the time the invention

was made to have substituted the KCl in Lauer et al's buffer with sodium sulfate because the substitution of art recognized equivalent salts for adjusting ionic strength, as shown by Ohmura et al, would have been within the skill of an artisan.

20. Claims 1, 3-5, 7-10, 12-21, 23-25, 27, 29, and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Keo et al, U.S. Patent 5,599,433.

With respect to claims 1, 20, 21, 23, 24, 25, 27, 29, and 33, Keo et al teaches the capillary zone electrophoresis (CZE) of glycosylated proteins in clinical specimens, wherein the buffer system is a solution that contains, for example, 100 mM CAPS, i.e., 3-cyclohecylamino-1-propanesulfonic acid (which reads on the instant zwitterionic biological buffer and additive), 300 mM sodium borate (which is a buffer), and NaOH for adjusting the pH to 11 (see col. 3, lines 32-55; col. 4, lines 43-49; col. 5, line 16 through col. 6, line 14; and col. 8, lines 32-43). It should be noted that CAPS is C_9 alkylsulfonate. Alternatively, the pH can be at 10 (see col. 10, line 46). It is noted that the instant specification teaches, at page 6, lines 17-20, that CAPS is an instant additive. The water in Keo et al's buffer system reads on the support in claim 24. The clinical specimen can be a human biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). These biological liquids, and in particular, the serum and plasma, inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. It is the Examiner's position that said CAPS buffer has a hydrophobic interaction with the albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin and provides these proteins with at least one negative charge thereby modifying the electrophorectic mobility.

With respect to claims 3 and 4, said serum, plasma, cerebrospinal fluid, or urine, etc, is a biological sample (see col. 6, lines 17-22).

With respect to claim 5, said albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin, in said serum or plasma, is a blood protein.

With respect to claims 7-10, said CAPS, which is a C_9 alkylsulfonate, has an anionic pole with a pH of more than 9 and a hydrophobic portion.

With respect to claim 12, the CAPS is present at a concentration of, example, 100 mM (see col. 6, lines 12-13), and it is the Examiner's position that this concentration does not exceed the critical micellar concentration of the CAPS.

With respect to claim 16, the pH can be 10 or 11 (see col. 6, line 14; and col. 10, line 46).

With respect to claim 17, a fused silica capillary tube is used (see col. 8, lines 21-22).

With respect to claims 18 and 19, and as noted above, the buffer contains NaOH for adjusting the pH (see col. 6, lines 13-14).

Keo et al teaches the limitations of the instant claims other than the differences which are discussed below.

With respect to claims 14 and 15, Keo et al does not specifically teach that its CAPS buffer concentration can be 1 mM to 4 mM, e.g., about 2.5 mM. Keo et al teaches that the CAPS buffer can be present at a concentration of about 10 mM to about 200 mM (see col. 6, lines 9-10). It is the Examiner's position that going slightly lower than the 10 mM concentration would have been within the skill of an artisan. It

would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a lower concentration of Keo et al's CAPS buffer, below the 10 mM concentration sated by Keo et al, i.e., to have used a CAPS buffer concentration of, for example 4 mM or 2.5 mM, to perform Keo et al's capillary zone electrophoresis, because the use of slightly lower concentrations of buffer would have been within the level of ordinary skill in the art.

Keo et al does not specifically require that said buffer system containing the CAPS, sodium borate, and NaOH be used for the serum, plasma, cerebrospinal fluid, or urine biological fluid. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used said buffer system containing CAPS, sodium borate, and NaOH for the serum, plasma, cerebrospinal fluid, or urine biological fluid because such is clearly within the scope of Keo et al's disclosure.

21. Claims 24 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al, U.S. Patent 4,769,408.

Ogawa et al prepares an aqueous solution comprising buffer and an anionic surfactant such as sodium dodecylsulfate (see col. 13, line 22 through col. 14, line 64; and Example 1 at cols. 15-16). Sodium dodecylsulfate, which is a C_{12} alkylsulfate, reads on the instant additive. The pH of the solution can be, for example, 10 (se col. 13, lines 41-42). The water in the solution reads on the support in claim 24. The recitation "for capillary electrophoresis" is merely intended use and is not deemed to be a positive limitation of the instant claims. Ogawa et al teaches the limitations of the instant claims other than the difference which is discussed below.

Ogawa et al does not specifically prepare its solution having a pH of 10 with said sodium dodecylsulfate. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Ogawa et al's solution having a pH of 10 with sodium dodecylsulfate because such is clearly within the scope of Ogawa et al's disclosure.

22. Claims 27, 29, and 33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ogawa et al as applied to claims 24 and 25 above, and further in view of Mullis et al (U.S. Patent 4,965,188).

Ogawa et al is relied upon for the reasons recited above. Ogawa et al further teaches that its buffer can be TAPS, i.e., N-[tris(hydroxymethyl)-methyl]-3-aminopropanesulonic acid (see col. 13, line 63-64), and that the pH can range from 2.5 to 10.0 (col. 13, lines 41-42). It should be noted that TAPS is a C_7 alkylsulfonate, is a zwitterionic biological buffer, and encompasses the instant additive. Ogawa et al teaches the limitations of instant claims 27, 29, and 33, the difference being that Ogawa et al does not specifically teach that TAPS can be used to buffer at a pH between 9 and 10. Mullis et al is relied upon for showing that TAPS can be used to buffer at pH 9.3 (see col. 36, line 12). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have used Ogawa et al's TAPS buffer to buffer at pH 9.3 because TAPS can be used to buffer at pH 9.3, as shown by Mullis et al.

23. Claims 24, 25, and 27-30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bellon et al (U.S. Patent 5,928,484) in view of Keyes (U.S. Patent 4,714,677) and Bloebaum et al (U.S. Patent 4,872,865).

Bellon et al teaches a buffer solution comprising Tris buffer and 1-hydroxy naphthalene 2-carboxylic acid (which reads on the instant additive) (see Example IV at col. 11). In place of said 1-hydroxy naphthalene 2-carboxylic acid, there can be used sodium cholate, sodium dodecylbenzenesulfonate, sodium dodecylsulfate, naphthalene 2-carboxylic acid, or naphthalene 2-sulfonic acid (which each read on the instant additive) (see col. 6, lines 10-55). Said 1-hydroxy naphthalene 2-carboxylic acid, sodium cholate, sodium dodecylbenzenesulfonate, sodium dodecylsulfate, naphthalene 2-carboxylic acid, and naphthalene 2-sulfonic acid are examples of Bellon et al's molecules that have a hydrophobic moiety (see col. 6, lines 10-55). In general, said molecule having a hydrophobic moiety can, for example, comprise a linear or branched aliphatic chain of 3 to 10 carbon atoms bearing a sulfonic acid function. It is the Examiner's position that this encompasses C_6 to C_{10} alkyl sulfonates, such as octanesulfonate. The pH can be at about 9, and it is the Examiner's position that said Tris buffer can buffer at a pH of about 9 (see col. 5, line 43). Bellon et al teaches the limitations of the instant claims other than the difference which is discussed below.

Bellon et al does not specifically require a pH of between 9 and 11 for its buffer solution, i.e., in Bellon et al's examples (see cols. 10 to 11) the pH is never given. However, as noted above, Bellon et al uses Tris buffer, and the pH can be about 9. Furthermore, Keyes (col. 17, lines 39-40 and 49) and Bloebaum et al (col. 6, line 33) are relied upon for showing that Tris can buffer at pH 9.1. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Bellon et al's buffer solution at a pH of about 9, such as 9.1 because Tris can buffer at

such a pH, as shown by Keyes and Bloebaum et al, and Bellon et al teaches a pH of about 9, as noted above.

Bellon et al does not specifically teach that its molecule having a hydrophobic moiety can be a C_6 to C_{10} alkyl sulfonates, such as octanesulfonate. However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to have used a C_6 to C_{10} alkyl sulfonates, such as octanesulfonate for Bellon et al's molecule having a hydrophobic moiety because Bellon et al teaches that its molecule having a hydrophobic moiety can comprise a linear or branched aliphatic chain of 3 to 10 carbon atoms bearing a sulfonic acid function.

Double Patenting

24. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

25. Claims 1-5, 7-25, 27-30, and 33 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4 and 8-28 of copending Application No. 10/052,601. Although the conflicting claims are not identical, they are not patentably distinct from each other because the

method claims in said copending application are anticipatory of the instant method claims, but are of a different scope. For example, claim 20 in said copending application teaches the use of octanesulphonate as an additive in the buffer for capillary electrophoresis. Claim 21 in said copending application teaches a concentration of 1 to 5 mM. Note that claim 1 in said copending application analyzes the same proteins as in instant claim 1. The biological buffer in claim 1 of said patent, such as CAPS, also reads on the instant additive. CAPS is a C_9 alkylsulfonate. When one prepares the buffer system in the method claims of said copending application, the instant solution will be obtained.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Response to Arguments

26. Applicant's arguments filed February 4, 2005 have been fully considered but they are not persuasive.

Applicant argues that there is no mention of serum proteins in Lauer et al, and thus, that Lauer et al cannot anticipate the instant claims 1, 20, and 21. However, this argument is not deemed to be persuasive because the proteins separated in Figure 2 at page 168 of Lauer et al include conalbumin and ovalbumin, which are "albumin" as in instant claims 1, 20, and 21. Instant claims 1, 20, and 21 do not require that the recited proteins are serum proteins.

Applicant argues that Ogawa et al describes aqueous gels that cannot be used as running buffers, and that the instant claims recite a buffer solution, not a gel.

However this argument is not deemed to be persuasive because Ogawa et al's gel-forming solution, prior to forming the gel, encompasses the instant solution (see col. 13, line 22 through col. 14, line 64; and Example 1 at cols. 15-16).

Applicant argues that Bellon et al describes aqueous gels and biological samples that are distinct from the buffer system as now claimed, and fails to teach or suggest the pH ranges claimed. However, this argument is not deemed to be persuasive because Bellon et al, in Example IV at col. 11, teaches a migration buffer comprising Tris buffer and 1-hydroxy naphthalene 2-carboxylic acid. This buffer is a solution of a buffer system as here claimed. With respect to pH, Bellon et al refers to a pH of about 9 (see col. 5, line 43). Furthermore, Keyes (col. 17, lines 39-40 and 49) and Bloebaum et al (col. 6, line 33) are relied upon for showing that Tris can buffer at pH 9.1. It would have been obvious to one of ordinary skill in the art at the time the invention was made to have prepared Bellon et al's buffer solution at a pH of about 9, such as 9.1 because Tris can buffer at such a pH, as shown by Keyes and Bloebaum et al, and Bellon et al teaches a pH of about 9, as noted above.

Applicant argues that Bellon et al concerns the analysis of Lp(a). However, this argument is not deemed to be persuasive because Bellon et al's migration buffer solution encompasses the instant solution, regardless of what is being analyzed.

Applicant argues that Keo et al does not teach or suggest the protein constituents in claims 1 and 21 (and also claim 20), and that Keo et al does not teach or suggest the additives now in claims 24 and 25. However, this argument is not deemed to be persuasive because the clinical specimen used by Keo et al can be a human

biological liquid such as serum, plasma, cerebrospinal fluid, urine, etc (see col. 6, lines 17-22). These biological liquids, and in particular, the serum and plasma, inherently contain the instant albumin, α_1-globulin, α_2-globulin, β-globulin, β_1-globulin, β_2-globulin, and γ-globulin. Furthermore, Keo et al's CAPS buffer, i.e., 3-cyclohecylamino-1-propanesulfonic acid reads on the instant zwitterionic biological buffer and additive. It should be noted that CAPS is C_9 alkylsulfonate. It is also noted that the instant specification teaches, at page 6, lines 17-20, that CAPS is an instant additive.

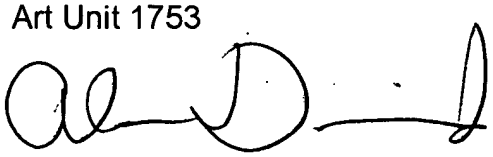
Applicant argues that the ionic strength adjuster in Omura et al is to precipitate albumin. However, this argument is not deemed to be persuasive because Ohmura et al clearly shows that salts for adjusting ionic strength include KCl and sodium sulfate (see the paragraph bridging cols. 7 and 8). It would have been obvious to one of ordinary skill in the art at the time the invention was made to have substituted the KCl in Lauer et al's buffer with sodium sulfate because the substitution of art recognized equivalent salts for adjusting ionic strength, as shown by Ohmura et al, would have been within the skill of an artisan. Nothing unexpected has been demonstrate by using conventional sodium sulfate in place of conventional KCl.

27. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Alan Diamond whose telephone number is 571-272-1338. The examiner can normally be reached on Monday through Friday, 5:30 a.m. to 2:00 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nam Nguyen can be reached on 571-272-1342. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Alan Diamond
Primary Examiner
Art Unit 1753



Alan Diamond
April 22, 2005